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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,241	01/17/2002	Bernhard Hauer	50531	6324

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/031,241	HAUER ET AL.	
	Examiner	Art Unit	
	YONG D. PAK	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,12,14-18 and 23-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,12,14-18 and 23-30* is/are rejected.

7)☐ Claim(s) _ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 of PCT/EP00/07251.

The amendment filed on March, 23, 2009, amending claims 14-15, has been entered.

Claims 11-12, 14-18, and 23-30 and are under consideration.

Claim Objection

Claim 15 is objected to because of the following informalities:

Claim 15 is objected for the recitation of “the amino acid sequence SEQ ID NO:35”. It appears that "of” has been inadvertently left out in front of “SEQ ID NO:35”.

Response to Arguments

Applicant’s amendment and arguments filed on March 23, 2009, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied.

Claim Rejections - 35 USC § 112-2nd paragraph

In view of the amendment of claims 14-15, the rejections of claims 14-15 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out

and distinctly claim the subject matter which applicant regards as the invention have been **withdrawn.**

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 11-12, 14, 16-18, and 23-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Estabrook et al. in view of Creaser et al., Fish et al., Reipa et al. and Oliver et al.

Claim 11-12, 14, 16-18, and 23-30 drawn to a method for the enzymatic production of terminally or subterminally hydroxylated fatty acids comprising hydroxylating fatty acids in the presence of an electro donor system, a cytochrome P450 monooxygenase or a mutant of a cytochrome P450 of SEQ ID NO:35 having a mutation at position 87, and oxygen, wherein said electron donor system is zinc dust/Co(III)sepulchrate.

Estabrook et al. (*Methods in Enzymology* – form PTO-1449) discloses a method for the enzymatic production of terminally or subterminally hydroxylated fatty acids comprising hydroxylating fatty acids in the presence of an electron donor system, a cytochrome P450 monooxygenase, oxygen, chloride ions and a hydrogen peroxide-

cleaving enzyme, wherein said fatty acid is a C-12 fatty acid and wherein said electron donor system comprises a Co(III)sepulchrate mediator of Creaser et al.. Estabrook, et al. teaches that said mediator "retains chirality during reversible oxidation-reduction" (page 45, 1st paragraph).

The difference between the reference of Estabrook et al. and the instant invention is that the reference of Estabrook et al. does not teach a method of producing terminally or subterminally hydroxylated fatty acids using a Zn metal in powder form as the source of non-electrode bound electrons or a mutant of a cytochrome P450 of SEQ ID NO:35 having a mutation at position 87.

Creaser et al. (J. Am. Chem. Soc – form 1449) discloses a Zn/Co(III)sepulchrate electron donor system, which pioneered for the use of Co(III)sepulchrate as mediators in electrochemical reactions (Faulkner et al. – form PTO-1449, Reipa et al. – US Patent 6,126,795 and Roberts et al. – US Patent 6,492,132), wherein the Co(III)sepulchrate mediator is the same mediator used by Estabrook et al. Creaser et al. teaches that Zn dust, a source of non-electrode bound electrons, causes reduction of the Co(III)sepulchrate mediator within seconds (page 3181).

Fish et al. (Talanta. 1997 May;44(5):939-45 - form PTO-892) dislcoses that interference of organic matter with electrode response is a been well known problem in the art (page 939) and offers methods to lessen said interference. Reipa et al. (US Patent No. 6,126,795 - form PTO-892) discloses disadvantages of a system using electrodes and P450 enzymes in hydroxylating organic compounds: irreversible

adsorption of protein constituents leading to electrode fouling and protein denaturation (Column 2, lines 34-55).

Oliver et al. (Biochemistry 1997, 36, 1567-1572 – form PTO-892) discloses a mutant of SEQ ID NO:35 having a F87A mutation which hydroxylates fatty acids at the ω position, unlike the wildltype enzyme (abstract and page 1567).

Therefore, in combining the teachings of Estabrook et al., Creaser et al., Fish et all, Reipa et al. and Oliver et al., it would have been obvious to one having ordinary skill in the art to modify the method of Estabrook et al. in hydroxylating fatty acids at the ω by using the mutant cytochrome P450 monooxygenase of Oliver et al. and using Zn dust as the non-electrode source of elections as taught by Creaser et al. One of ordinary skill in the art would have been motivated to use the mutant cytochrome P450 monooxygenase of Oliver et al. because said mutant is able to catalyze ω hydroxylation of fatty acids. One of ordinary skill in the art would have been motivated to use Zn dust as a source of non-electrode bound electrons because Creaser et al. teaches that Zn dust causes immediate reduction, Zn dust is widely available (Sigma), Reipa et al. teaches disadvantages of a system using electrodes and P450 enzymes in hydroxylating organic compounds (irreversible adsorption of protein constituents leading to electrode fouling and protein denaturation) thus decreasing it's efficacy, and Fish et al. teaches that electrode fouling due to organic matter is a problem well known in the art. One of ordinary skill in the art would have had a reasonable expectation of success since Estabrook et al. teaches a method of hydroxylating fatty acids with cytochrome P450 monooxygenases by replacing NADPH with an electrochemically generated

reduction by the mediator Co(III)sepulchrate, Creaser et al. teaches a method of generating two electrons using the mediator Co(III)sepulchrate and Zn dust as the source of electrons, and Oliver et al. teaches a mutant that catalyzes ω hydroxylation of fatty acids.

Therefore, the above references render claims 11-12, 14, 16-18, and 23-30 *prima facie* obvious to one of ordinary skill in the art. Applicants should note that the rejection has been amended.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 11-12, 14-18, and 23-30 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 7,531,335 in view of Estabrook et al., Creaser, Fish et al., and Reipa et al.

U.S. Patent No. 7,531,335 discloses a process for the enzymatic production of terminally or subterminally hydroxylated fatty acids comprising hydroxylating fatty acids in the presence of variant of the P450 monooxygenase of SEQ ID NO:2, wherein the variant has a F87A or F87V, L188K, A74G, R47F, and V26T. SEQ ID NO:2 and SEQ ID NO:35 of the instant application are 100% identical.

The difference between the reference of U.S. Patent No. 7,531,335 and the instant invention is that U.S. Patent No. 7,531,335 does not teach a method of producing terminally or subterminally hydroxylated fatty acids using a Zn metal in powder form as the source of non-electrode bound electrons.

Estabrook et al. (*Methods in Enzymology* – form PTO-1449) discloses a method for the enzymatic production of terminally or subterminally hydroxylated fatty acids comprising hydroxylating fatty acids in the presence of an electron donor system instead of using NADPH or NADH, a cytochrome P450 monooxygenase, oxygen, chloride ions and a hydrogen peroxide-cleaving enzyme, wherein said fatty acid is a C-12 fatty acid and wherein said electron donor system comprises a Co(III)sepulchrate mediator of Creaser et al.. Estabrook, et al. teaches that said mediator "retains chirality during reversible oxidation-reduction" (page 45, 1st paragraph).

Creaser et al. (J. Am. Chem. Soc – form 1449) discloses a Zn/Co(III)sepulchrate electron donor system, which pioneered for the use of Co(III)sepulchrate as mediators

in electrochemical reactions (Faulkner et al. – form PTO-1449, Reipa et al. – US Patent 6,126,795 and Roberts et al. – US Patent 6,492,132), wherein the Co(III)sepulchrate mediator is the same mediator used by Estabrook et al. Creaser et al. teaches that Zn dust, a source of non-electrode bound electrons, causes reduction of the Co(III)sepulchrate mediator within seconds (page 3181).

Fish et al. (Talanta. 1997 May;44(5):939-45 - form PTO-892) dislcoses that interference of organic matter with electrode response is a been well known problem in the art (page 939) and offers methods to lessen said interference. Reipa et al. (US Patent No. 6,126,795 - form PTO-892) discloses disadvantages of a system using electrodes and P450 enzymes in hydroxylating organic compounds: irreversible adsorption of protein constituents leading to electrode fouling and protein denaturation (Column 2, lines 34-55).

Therefore, in combining the teachings of Estabrook et al., Creaser et al., Fish et al., and Reipa et al. it would have been obvious to one having ordinary skill in the art to modify the method of US Patent 7,531,335 by hydroxylating fatty acids at the ω by using the electron donor system taught by Estabrook and using Zn dust as the non-electrode source of elections as taught by Creaser et al. One of ordinary skill in the art would have been motivated to use the above described electron donor system instead of using NADPH or NADH. One of ordinary skill in the art would have been motivated to use Zn dust as a source of non-electrode bound electrons because Creaser et al. teaches that Zn dust causes immediate reduction, Zn dust is widely available (Sigma), Reipa et al. teaches disadvantages of a system using electrodes and P450 enzymes in

hydroxylating organic compounds (irreversible adsorption of protein constituents leading to electrode fouling and protein denaturation) thus decreasing it's efficacy, and Fish et al. teaches that electrode fouling due to organic matter is a problem well known in the art. One of ordinary skill in the art would have had a reasonable expectation of success since Estabrook et al. teaches a method of hydroxylating fatty acids with cytochrome P450 monooxygenases by replacing NADPH with an electrochemically generated reduction by the mediator Co(III)sepulchrate, Creaser et al. teaches a method of generating two electrons using the mediator Co(III)sepulchrate and Zn dust as the source of electrons, and Oliver et al. teaches a mutant that catalyzes ω hydroxylation of fatty acids.

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

/Yong D Pak/
Primary Examiner, Art Unit 1652